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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/542,555 | 08/29/2005 | Erik Schwiebert | EL970613375US | 7032 |
| 23859 | 7590 | 09/01/2006 | EXAMINER | |
| NEEDLE & ROSENBERG, P.C. SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30309-3915 | | | | PAK, JOHN D |
| | | ART UNIT | | PAPER NUMBER |
| | | 1616 | | |

DATE MAILED: 09/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/542,555 | SCHWIEBERT ET AL. | |
| | Examiner | Art Unit | |
| | JOHN PAK | 1616 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 14 August 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-3, 12, 13, 21-23, 37, 38, 41-45, 48-52, 58, 61 and 64 is/are pending in the application.
- 4a) Of the above claim(s) 37, 38, 41-45, 48-52, 58, 61 and 64 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-3, 12, 13 and 21-23 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 7/8/05 is/are: a) accepted or b) objected to by the Examiner. — See PTO-948
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
 Paper No(s)/Mail Date 2/06.
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

Claims 1-3, 12-13, 21-23, 37-38, 41-45, 48-52, 58, 61 and 64 are pending.

Applicant's election with traverse of the invention of Group I in the reply filed on 8/14/2006 is acknowledged. Applicant traverses the lack of unity requirement because "the claims all include administering zinc to a cell" and "this constitutes a special technical feature that defines a contribution that the claimed subject matter makes over the prior art." Applicant submits that U.S. Patent 5,840,278 discloses administering zinc in the amount of 35 mg, which is more than 10 times the preferable amount disclosed by applicant, 1.3-2.6 mg; and therefore, applicant argues, the '278 patent does not anticipate the claims and the inventions possess a unity of invention.

The Examiner cannot agree. Applicant's specification page 25 discloses:

- 15 The terms "effective amount" and "effective dosage" are used interchangeably. The term "effective amount" is defined as any amount necessary to produce a desired physiologic response. Effective amounts and schedules for administering the compositions may be determined empirically, and making such determinations is within the skill in the art. The dosage ranges for the administration
- 20 of the compositions are those large enough to produce the desired effect in which the symptoms of the disorder are affected. The dosage should not be so large as to cause adverse side effects, such as unwanted cross-reactions, anaphylactic reactions, and the like. Generally, the dosage will vary with the age, condition, sex and extent of the disease in the patient, route of administration, or whether other drugs are
- 25 included in the regimen, and can be determined by one of skill in the art. The dosage can be adjusted by the individual physician in the event of any counterindications. Dosage can vary, and can be administered in one or more dose administrations daily, for one or several days. Guidance can be found in the literature for appropriate dosages for given classes of pharmaceutical products.

Apparently, the amount of administered zinc is "any amount necessary to produce a desired physiologic response," dosages "can vary," and "[g]uidance can be found in the literature for appropriate dosages for a given classes of pharmaceutical products." Furthermore, the claims read on treatment of many different diseases, including the common cold, the subject of the aforementioned '278 patent. See applicant's specification page 32:

The methods of the present invention are useful in various diseases, infections, and conditions. Zinc is anti-inflammatory and is protective in asthma and other airway diseases or ailments, including common cold. Zinc, given in the solution described herein, also has unique applications to be anti-inflammatory by 10 entering mammalian cells and inhibiting inflammatory signaling cascades with the cell (by blocking induction of the key transcription factor NFkappaB) and by affecting the growth and/or metabolism of a wide variety of bacterial pathogens through competitive inhibition of metal scavenging pathways essential for bacterial pathogen survival and growth in the host.

Hence, applicant's invention uses the same zinc and treats the same disease. Moreover, applicant's invention is quite broad in treating various other diseases, infections and conditions. Applicant's argument as to different dosage is found most unpersuasive for these reasons alone.

However, there is another compelling reason why applicant's argument is unpersuasive. Applicant seems to believe that the 35 mg zinc in the '278 patent is to be administered in a single dose. The Examiner queries where in the '278 patent such a disclosure can be found. The exemplified zinc-containing nasal spray composition in the '278 patent is not disclosed as a unit dosage composition. One skilled in the art

would have recognized just from the volume of the composition, 1.5 fluid ounces (more than 44 ml), that the nasal spray was being disclosed as a product, not a single shot spray. For example, in U.S. Patent 5,622,724, dose for a zinc ion containing nasal spray is 0.05-0.5 ml, which is close to 900 times smaller in dose volume than applicant's asserted 1.5 fluid ounces. Indeed, for 1.5 fluid ounces to be used up in one single spray dose, the user would have to spend a significant amount of time to squeeze the spray bottle dozens or even hundreds of times and suffer large volumes of run-off, etc. Clearly, 1.5 fluid ounces for a nasal spray dose would not have been reasonably recognized by the skilled artisan in the absence of clear disclosure to the contrary. Additionally, the way that the independent claim 3 in the '278 patent is recited in terms of volume percentages conveys the meaning that a nasal spray per se was being disclosed, not a unit dose composition.

For these reasons, applicant's traversal of the lack of unity requirement is found unconvincing. For the reasons stated above and for the reasons of record, the finding of lack of unity is still deemed to be proper and is hereby maintained and made FINAL. Accordingly, claims **1-3, 12-13 and 21-23** will presently be examined *to the extent that* they read on the administration of Zn⁺², and claims **37-38, 41-45, 48-52, 58, 61 and 64** and the amended subject matter of claims 1-3, 12-13 and 21-23 wherein the administered agent is not Zn⁺² are withdrawn from further consideration as being directed to non-elected subject matter. Applicant's amendment of claims 1 and 12 to include other alternative ingredients shall have no bearing on the elected invention of

Group I, the subject of which was clearly and expressly set forth in the Office action of 7/11/2006. Applicant's election of Group I necessitates the first examination on the merits of this application based on the elected subject matter.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 12-13, and 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Coleman (US 5,840,278).

Coleman explicitly discloses administering via aqueous nasal spray a composition that contains, *inter alia*, 35 mg zinc, 106 mg calcium, and sodium bicarbonate in 1.5 fluid ounces (see from column 1, line 42 to column 2, line 7; see also claims 1-5).

The presence of sodium bicarbonate meets the "alkalinized" feature of dependent claims. "High Ca²⁺" claim feature is met by the presence of calcium. Use of zinc by Coleman meets the "P2X receptor agonist" claim feature because zinc is one such agonist.

Even though "increasing cytosolic Ca²⁺ levels in an airway epithelial cell," "contacting P2X receptors on the cell," "contacting epithelial cells in the trachea, bronchi, bronchioles, or alveoli" and other similar claim language steps are not

expressly stated by Coleman in verbatim language, such steps would have been inherently produced by Coleman's method. Coleman delivers a nasal spray that contains in proportions 35 mg zinc and 106 mg calcium per 1.5 fluid ounces, which would clearly contact epithelial cells in claim-required areas. Once that contact is made, the very same zinc would necessarily function in the same way as now claimed by applicant. Since the same exact substance is delivered to the same exact substrate at an amount that cannot be distinguished, the same biomechanism and same end result (treatment) would necessarily be obtained. The claims are thereby anticipated.

Claims 1-3, 12-13, 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Bryce-Smith (US 5,622,724).

Bryce-Smith discloses treating symptoms of the common cold by administering a spray of a solution containing symptom effective treating amount of a solution of substantially unchelated ionic zinc compound to the nostrils and respiratory tract of a patient in need thereof (claim 1). The zinc ions are in a concentration of from about 0.004 to 0.12 w/v% (claim 1). Zinc chloride is specified (claim 7).

Even though "increasing cytosolic Ca²⁺ levels in an airway epithelial cell," "contacting P2X receptors on the cell," "contacting epithelial cells in the trachea, bronchi, bronchioles, or alveoli" and other similar claim language steps are not expressly stated by Bryce-Smith in verbatim language, such steps would have been inherently produced by Bryce-Smith's method. Bryce-Smith delivers a nasal spray that

contains 0.004-0.12 w/v% of zinc ions in the form of zinc chloride, which would clearly contact epithelial cells in claim-required areas. Once that contact is made, the very same zinc would necessarily function in the same way as now claimed by applicant. Since the same exact substance is delivered to the same exact substrate at an amount that cannot be distinguished, the same biomechanism and same end result (treatment) would necessarily be obtained.

Applicant's claims 12 and 21 are noted, but Bryce-Smith does not recite any magnesium in his aqueous solution (claim 2), so at least the feature of Zn⁺² containing solution with low Mg⁺² is met. Applicant's claim 22 is noted -- the feature of performing the contacting step with a Zn⁺² containing inhalant or nebulization is squarely met by the nasal spray disclosure of Bryce-Smith.

For these reasons, the claims are anticipated.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 12-13, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Taylor et al., Schwiebert et al. (American Journal of Physiology, June 2001) and CAPLUS abstract 2001:30580.

Taylor et al. disclose that P2X purinergic receptor channels bind ATP and mediate Ca^{2+} influx and signals that stimulate secretory Cl^- transport across epithelia (abstract and Discussion section on pages 882-884). P2X receptors can be targeted to treat cystic fibrosis (p. 875, right column, last sentence of first paragraph).

Schwiebert et al. disclose that P2X receptors, on binding their ATP ligand, may increase cytosolic Ca^{2+} transiently and stimulate Cl^- and fluid secretion and ciliary beat frequency (Figure 2 on page F949). Purinergic agonists have been used to stimulate Cl^- and fluid secretions from cystic fibrosis tissues and epithelial cell models from the lung and airways and from the GI systems (page F957, last paragraph). In cystic fibrosis, Cl^- and fluid secretion are lacking but sodium absorption is augmented (*id.*). Purinergic agonist therapy is disclosed to potentially correct the abnormal handling of salt and water by the respiratory epithelium (p. F958, right column, first six lines; see also Figure 7).

CAPLUS abstract 2001:30580 is cited to establish that zinc ion is a known P2X receptor modulator that potentiates the actions of ATP in P2X receptor gated ion channels.

Given the teachings of treating cystic fibrosis with P2X receptor agonists, the ordinary skilled artisan in this field would have been motivated to utilize the known agonist, zinc ion, to treat cystic fibrosis. Combined therapy with ATP is suggested from their coaction on the ion channels to bring about increased Cl^- transport and increased Ca^{2+} . Zinc chloride is suggested from its common availability as a zinc ion source. High

calcium concentration is suggested from the known effect of calcium to activate epithelial chloride channels. In cystic fibrosis, sodium absorption is augmented, so lower sodium concentration in the treatment medium is suggested. Lower magnesium in the treatment is suggested in order to control one more variable in the complicated cascade of factors. The ordinary skilled artisan would have been motivated to deliver the treatment composition via conventional means to access the target cystic fibrosis diseased cells, e.g. via nasal spray, nebulizer or aerosol inhaler.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teachings of the cited references.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620**. The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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